

AMENDMENTS TO THE CLAIMS

Claim 1 (currently amended): A ~~non-human~~ transgenic mouse animal whose genome comprises a first nucleotide sequence encoding human CD20 and a second nucleotide sequence encoding a subunit of a heterologous Fc γ III receptor, wherein the first nucleotide sequence is operably linked to an endogenous CD20 promoter, and wherein the second nucleotide sequence is operably linked to an endogenous Fc γ III receptor promoter.

Claim 2 (currently amended): The transgenic mouse animal of claim 1 wherein said endogenous CD20 promoter is first nucleotide sequence is operably linked to a human endogenous promoter.

Claim 3 (currently amended): The transgenic mouse animal of claim 2 whose cells express human CD20.

Claim 4 (currently amended): The transgenic mouse animal of claim 3 wherein human CD20 is expressed on the surface of B lymphocytes.

Claim 5 (currently amended): The transgenic mouse animal of claim 2, wherein said endogenous Fc γ III receptor promoter is second nucleotide sequence is operably linked to a human endogenous promoter.

Claim 6 (currently amended): The transgenic mouse animal of claim 1 wherein said second nucleotide sequence encodes human CD16 alpha chain subtype A.

Claim 7 (currently amended): The transgenic mouse animal of claim 6 wherein said receptor is expressed on the surface of leucocytes.

Claim 8 (currently amended): The transgenic mouse animal of claim 1 7 wherein said

receptor is expressed on the surface of one or more cells selected from the group consisting of a cell comprising NK cells, macrophages, neutrophils, eosinophils, basophils, mast cells, and or thymocyte cells or mixtures thereof.

Claim 9 (currently amended): The transgenic mouse animal of claim 1 wherein the genome of said mouse animal further comprises a disruption in an endogenous gene encoding a subunit of a receptor substantially homologous to the heterologous Fc γ III receptor.

Claim 10 (currently amended): The transgenic mouse animal of claim 9, wherein the endogenous gene encodes a murine CD16 alpha chain.

Claim 11 (withdrawn–currently amended): A method of identifying an agent capable of treating a B cell lymphoma said method comprising:

- a) measuring the level of B lymphocytes expressing human CD20 in a mouse an animal of claim 1;
- b) administering said agent to the mouse animal of claim 1; and
- c) measuring the level of B lymphocytes expressing human CD20 in the mouse animal; wherein a decrease in the number of B lymphocytes expressing human CD20 in the mouse animal after treatment with the agent identifies the agent capable of treating a B cell lymphoma.

Claim 12 (withdrawn): An agent identified according to claim 11.

Claim 13 (withdrawn–currently amended): A method of identifying an agent capable of depleting or killing cells expressing human CD20 said method comprising:

- a) measuring the level of B lymphocytes expressing human CD20 in a mouse an animal of claim 1;
- b) administering said agent to the mouse animal of claim 1; and
- c) measuring the level of B lymphocytes expressing human CD20 in the mouse animal;

wherein a decrease in the number of B lymphocytes expressing human CD20 in the mouse animal identifies the agent as capable of depleting or killing cells expressing CD20.

Claim 14 (withdrawn): The method of claim 13 wherein said cells are cancer cells.

Claim 15 (withdrawn): An agent identified according to claim 14.

Claim 16 (currently amended): A cell or tissue derived from the transgenic mouse animal of claim 1.

Claim 17 (cancelled)

Claim 18 (cancelled)

Claim 19 (withdrawn–currently amended): A method of identifying an agent capable of inducing an Fc-mediated effector cell response said method comprising

- a) measuring the baseline level of one or more cytokines associated with an Fc-mediated effector cell response in a transgenic mouse animal of claim 1;
- b) administering said agent to the transgenic mouse animal;
- c) measuring the level of the cytokines in the mouse animal;

wherein an increase in the level of cytokines after administration identifies the agent as capable of inducing an Fc-mediated effector cell response.

Claim 20 (withdrawn–currently amended): A method of identifying an agent capable of inducing an Fc-mediated effector cell response against B lymphocytes expressing human CD20, said method comprising:

- a) measuring the level of B lymphocytes expressing human CD20 in a first transgenic mouse animal;

- b) administering said agent to the first transgenic mouse animal;
- c) measuring the level of B lymphocytes expressing human CD20 in the first transgenic mouse animal;
- d) determining the percent reduction in the level of B lymphocytes between step (a) and step (c);
- e) measuring the level of B lymphocytes expressing human CD20 in a second transgenic mouse animal of claim 1;
- f) administering said agent to the second transgenic mouse animal of claim 1;
- g) measuring the level of B lymphocytes expressing human CD20 in the second transgenic mouse animal; and
- h) determining the percent reduction in the level of B lymphocytes between step (e) and step (g);

wherein if the percent reduction determined in step (h) is greater than the percent reduction determined in step (d), the agent is identified as capable of inducing an Fc-mediated effector cell response against B lymphocytes expressing human CD20.

Claim 21 (withdrawn–currently amended): A method of testing safety of anti- human CD20 therapy, said method comprising:

- a) measuring the level of B lymphocytes expressing human CD20 in a mouse an animal of claim 1;
- b) administering said agent to the mouse animal of claim 1; and
- c) measuring the level of B lymphocytes expressing human CD20 in the mouse animal; wherein a decrease in the number of B lymphocytes expressing human CD20 in the mouse animal identifies the agent as capable of depleting or killing cells expressing CD20;
- d) monitoring monitering the mouse animal for short or long term adverse effects.

Claim 22 (withdrawn–currently amended): A method of testing efficacy of anti- human CD20 therapy, said method comprising:

- a) measuring the level of B lymphocytes expressing human CD20 in a set of mice ~~animals~~ of claim 1;
- b) administering to each mouse ~~animal~~ of the set a different dose of an agent; and
- c) measuring the level of B lymphocytes expressing human CD20 in the mouse ~~animal~~ after each dose; and
- d) determining at least one dose of the agent that results in the most B cell depletion.

Claim 23 (new): The transgenic mouse of claim 1 wherein the first nucleotide sequence is operably linked to a murine endogenous promoter.

Claim 24 (new): The transgenic mouse of claim 1 wherein the second nucleotide sequence is operably linked to a murine endogenous promoter.

Claim 25 (new): The cell or tissue of claim 16 wherein the cell or tissue expresses human CD20.

Claim 26 (new): The cell or tissue of claim 16 wherein the cell or tissue expresses a subunit of human Fc γ III receptor.

Claim 27 (new): The transgenic mouse of claim 9 wherein the human CD20 is expressed on the surface of B lymphocytes and human CD16 alpha chain subtype A is expressed on the surface of leucocytes in the transgenic mouse.